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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,296	01/20/2006	Maria Acelia Marrero Miragaya	976-28 PCT/US	3363

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EXAMINER	
MACAULEY, SHERIDAN R	
ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,296	MARRERO MIRAGAYA ET AL.	
	Examiner	Art Unit	
	SHERIDAN R. MACAULEY	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-28 and 33-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-28 and 33-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A response and amendment were received and entered on February 5, 2010. All evidence and arguments have been fully considered. Claim 1-25 and 29-32 are cancelled. Claims 26-28 and 33-35 are pending and examined on the merits in this office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 26-28 and 33-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions consisting essentially of the thrombolytic proteins recited in the claims for the treatment of hemorrhoid disease, does not reasonably provide enablement for compositions for the reduction of pain, swelling and itching due to hemorrhoid disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or practice the invention commensurate in scope with these claims.

4. In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the instant case, those factors deemed most relevant are the amount of direction and guidance presented, the presence or absence of working examples and the nature of the invention.

5. The claims are drawn to a method for treating hemorrhoid disease in a human in need thereof, comprising administering to said human an effective amount of a pharmaceutical composition, said composition consisting essentially of a thrombolytic protein selected from the group consisting of tissue-type plasminogen activator (t-PA), urokinase (u-PA), streptokinase (SK), or a combination thereof, wherein the pharmaceutical composition is administered rectally, and wherein the pharmaceutical is effective to reduce pain, itching or swelling due to hemorrhoid disease. Further claimed embodiments include that the pharmaceutical composition consists essentially of recombinant SK and a carrier or excipient, wherein the concentration of SK is 50,000 to 1,500,000 IU per gram of pharmaceutical composition, and that the composition is administered as a suppository. The claims also recite a method for treating hemorrhoid disease in a human in need thereof, comprising administering to said human an effective amount of a pharmaceutical composition, said composition consisting essentially of a thrombolytic protein selected from the group consisting of tissue-type plasminogen activator (t-PA), urokinase (u-PA), streptokinase (SK), or a combination

thereof, EDTA, and sodium diclofenac, or sodium salicylate., wherein the pharmaceutical composition is administered rectally, and wherein the pharmaceutical is effective to reduce pain, itching or swelling due to hemorrhoid disease.

6. The disclosure is not enabling for the reduction of pain, swelling and itching due to hemorrhoid disease because it does not present enough direction and guidance for one skilled in the art to use the invention with a reasonable expectation of success without undue experimentation. The disclosure does not provide any guidance or working examples to direct one to use the invention such that it would be effective to reduce pain, swelling and itching due to hemorrhoid disease. The working examples disclosed in the instant application are directed to the treatment of hemorrhoid disease, but it is unclear whether the composition has been shown to reduce pain, itching and swelling. Examples 2, 4 and 6 are directed to the administration of the compositions of the claims. In example 2, compositions comprising t-PA are administered to rabbits and it is determined that the compositions do not cause rectal irritation. The compositions used in example 2 are prepared in example 1, which states that SK is also tested, but since all of the compositions prepared in example 1 appear to contain t-PA, it is unclear how the suitability of SK in the composition is tested. Further, it appears that the compositions prepared in example 1 are also used in example 4, although the components of the compositions are not clearly set forth. It is stated that figure 4 depicts the results of the experiments conducted in example 4, but the text describes comparisons to a control group but it is unclear how the results shown in figure 4 compare to the controls. Absent this evidence, it is not clear whether a composition

consisting essentially of a thrombolytic protein would be effective to reduce pain, itching or swelling due to hemorrhoid disease, particularly since, in figure 4, the most effective results are achieved using a composition consisting essentially of the protein, sodium salicylate and EDTA and, without any composition absent the protein to compare these results to, it is unclear whether the composition consisting essentially of the protein would be effective. Further, in example 6, applicant demonstrates that there are some clinical results achieved using the compositions consisting essentially of SK and t-PA. Although some reduction in pain, itching and swelling is shown, applicant sates that the results were not statistically significant. Also, these results are only shown with specific suppositories comprising SK and t-PA. No experimental evidence is shown using compositions comprising u-PA, and no evidence is shown using different amounts of SK or t-PA in a suppository. Thus, there is nothing to direct one of ordinary skill in the art regarding the dosage of the proteins that would be safe or effective for one of ordinary skill in the art to administer in a suppository.

7. Further, the state of the prior art indicates that, at the time of application, the administration of a composition consisting essentially of a thrombolytic protein for the reduction of pain, swelling and itching may have been unsafe or ineffective at the time of the invention. Eschenfelder (US 4,944,943; reference cited in prior action) states that the addition of an antithrombotic substance is necessary to safely treat hemorrhoidal thrombosis (col. 2, lines 30-41). Further, Bachmann (J. Lab. Clin. Med. 1968, 72:228-238; document cited in IDS) teaches that the amounts of streptokinase recited in the claims are ineffective because they are not absorbed at the levels necessary to give a

thrombolytic response in human plasma (p. 229, par. 1-2). Given these facts, one skilled in the art would be unable to predict whether a composition consisting essentially of the ingredients recited in the claims could be used to reduce pain, swelling or itching in hemorrhoid disease without undue experimentation or with a reasonable expectation of success.

8. Therefore, the disclosure of the instant application does not enable one skilled in the art to use or practice the invention as claimed.

Claim Rejections - 35 USC § 103

9. Rejections under 35 USC 103 have been withdrawn due to applicant's amendment.

Response to Arguments

10. Applicant's arguments with respect to the previous rejections under 35 USC 103 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHERIDAN R. MACAULEY whose telephone number is (571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM
/Ruth A. Davis/
Primary Examiner, Art Unit 1651